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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/798,096	03/11/2004	Rea-Min Chu	P/741-176	6503

2352 7590 04/05/2007
OSTROLENK FABER GERB & SOFFEN
1180 AVENUE OF THE AMERICAS
NEW YORK, NY 100368403

EXAMINER	
BERTOGLIO, VALARIE E	
ART UNIT	PAPER NUMBER
1632	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/05/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/798,096	CHU ET AL.	
	Examiner	Art Unit	
	Valarie Bertoglio	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01/10/2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's reply dated 01/10/2007 has been received. Claims 1-16 have been cancelled. Claims 17 and 22 have been amended. Claim 28 has been added. Claims 17-28 are pending and under consideration in the instant office action.

Claim Objections

The objections to the claims are withdrawn in light of Applicant's cancellation of the claims.

The objection to claim 22 is withdrawn with respect to the removal of the word "and" and the insertion of the word "wherein". However, the objection is maintained as it relates to limiting the plasmid to a pcDNA3.1 vector as the way the claim is written, it appears as though Applicant is inadvertently limiting the plasmid to a vector without the necessary DNA sequences encoding IL-6 and IL-15. The phrase "a pcDNA3.1/V5-His-TOPO vector" could be interpreted to exclude the other limitations of the claim. Appropriate correction is required.

Claim Rejections - 35 USC § 112-1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 17-27 remain rejected and newly added claim 28 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a therapeutic composition for inhibiting tumor cells producing TGF-β, comprising a plasmid comprising SEQ ID NO:1 encoding IL-6 and a plasmid comprising **SEQ ID NO:4** encoding IL-15 operably linked to an IL-2 signal peptide, and a method of inhibiting the growth of the TGF-β producing tumor cells by administering the plasmids via muscle electroporation, does not reasonably provide enablement for a therapeutic composition comprising

a plasmid comprising SEQ ID NO:1 encoding IL-6 and a plasmid comprising SEQ ID NO:3 encoding IL-15 without operable linkage to an IL-2 secretion signal sequence, or 2) a method of inhibiting the growth of any tumor cells. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. The rejection is maintained for reasons originally set forth at pages 3-9 of the office action dated 08/26/2005. The maintained grounds of the rejection are reiterated below.

The claims are drawn to a composition for gene therapy, comprising a plasmid comprising SEQ ID NO:1, encoding IL-6 and a plasmid encoding SEQ ID NO:3, encoding IL-15, used for treating tumor cells such as CTVT, wherein the composition antagonizes TGF-β and activates NK cells to inhibit the growth of tumor cells, and a method for gene therapy, comprising inhibiting tumor cell growth, such as CTVT with said composition.

The specification provides guidance on the manufacture of two plasmids: one comprising a sequence encoding human IL-6 (SEQ ID NO:1); and the second comprising a sequence encoding human IL-15 operably linked to the human IL-2 signal peptide (**SEQ ID NO:4**; specification, pg. 10, pgph 40). It is noted that the claimed SEQ ID NO:3 is a DNA encoding IL-15 without the IL-2 signal sequence. No other plasmids are disclosed as a therapeutic composition. Further, the specification teaches that when the plasmids are electroporated into CB-17 mice, seven days after the mice were injected with xenogeneic CTVT tumors, the tumors showed a decrease in tumor size at day 14 in comparison to mock controls. Based on these *in vivo* results applicant's claim their instant invention.

Applicant's arguments have been fully considered and are not persuasive. Applicant argues that the claims have been amended to more clearly define the invention and now recite that the DNA encoding IL-15 is linked to a signal peptide. Claim 28 is limited to an IL-2 signal peptide that is merely linked, and is not necessarily operably linked, to the DNA encoding IL-15. It is noted that Applicant states that claim

22 has been amended but it appears that this remark is made in reference to claim 17 as the amendments discussed pertain to claim 17 and not to claim 22 (see page 5, last paragraph of Applicant's Remarks).

Claim 17 remains broad and is not enabled by the specification as it fails to require operable linkage to a signal peptide and the signal peptide is not limited to the IL-2 secretion signal peptide as taught by the specification. Claim 22 has not been amended to require any signal peptide.

Previously, claim 1 recited use of IL -15 whereas the specification taught use if IL-15 operably linked to a signal sequence from IL2. Claim 17 recites SEQ ID NO:3, which encodes IL -15 alone, and does not include the IL-2 signal peptide, which is present in the plasmid used in the instant invention. While the specification fails to explain the purpose of the signal peptide, a review of the literature demonstrates that an IL2SP/IL15 fusion protein is secreted as a result of the presence of the IL2SP. The instant invention appears to necessitate the secretion of IL15 for its function. Applicant has amended claim 17 to require linkage of IL-15 to a signal peptide, however, this breadth of signal peptides is not supported by the specification and the claim continues to fail to require an operable linkage. The term "linked" is not defined by the specification and encompasses spatial linkage of the DNAs, not necessarily linkage of the encoded polypeptides such that they are operable as a unit.

Furthermore, it is noted that, as taught by Suzuki et al., not all secretion signal peptides work at the same efficiency. In fact, the natural secretion signal peptide of IL-15 is inefficient and thus replaced with that of IL-2 (see page 532, col. 1, paragraph 1 and page 533, col. 2, paragraph 1). The only signal peptide contemplated by the specification is the IL-2 signal peptide as defined at paragraph [0040] of the specification (page 10). It is noted that the claims broadly encompass other types of signal peptides, including those that signal events other than secretion, that are not supported by the specification.

Claim Rejections - 35 USC § 112-2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 22-27 remain rejected and claims 17-21 and 28 are newly rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 22 remains incomplete as written. The preamble of the claim is drawn to a method of inhibiting growth of tumor cells. However, the claim is incomplete because the method steps do not relate back to the preamble in a positive process. The claim does not require obtaining an effect that is indicative of inhibition of tumor growth. Appropriate correction is required. Claims 23-27 depend from claim 22.

The above rejection was inadvertently omitted, in part, in the previous office action. As a result, the rejection is maintained, however, the action is being made non-final so that Applicant has due chance to respond.

The following new rejection is necessitated by amendment.

Claim 17 is unclear in that it now reads that the DNA sequence of SEQ ID NO:3 encoding IL-15 is linked to a signal peptide. The claim reads as though SEQ ID NO:3 is linked to a signal peptide, which is not consistent with what is taught in the specification. Thus, it is not clear whether the DNA sequence of SEQ ID NO:3 is linked to a peptide or the protein encoded by the DNA encodes IL15 linked to a peptide. Neither interpretation is consistent with the teachings in the specification. SEQ ID NO:3 does not encode a protein with a signal peptide. Claims 18-28 depend from claim 17. As written, because the claim refers to SEQ ID NO:3, as opposed to SEQ ID NO:4, it is referring to a DNA sequence encoding only IL-15. Claims 18-21 and 28 depend from claim 17.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Valarie Bertoglio whose telephone number is (571) 272-0725. The examiner can normally be reached on Mon-Thurs 5:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

PETER PARAS, JR.
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Valarie Bertoglio
Examiner
Art Unit 1632